REMARKS

The Office Action of August 29, 2005, which replaces and supercedes the Office Action of July 12, 2005, and the cited and applied reference have been carefully reviewed. No claim is allowed. Claims 1-4 and 6-12 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The examiner suggested that the priority data be updated in the first sentence of the specification. The "Cross-Reference to Related Applications" section with the updated priority data is moved ahead of the "Government License Rights" section so that the first sentence of the specification is directed to the priority claim.

Claims 1-4 and 6-12 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The examiner states that the claims are not limited to transactivation because assay A in claim 1 still recites treating neuronal cells with a candidate small molecule "activator" instead of a "transactivator". Applicants had intended in the previous amendment to correct all instances of "activator" to "transactivator" and had simply overlooked the above exception. Applicants regret the confusion caused by this oversight. The claims are now amended to be directed to only "transactivation"

(i.e., all instances of "activator" are replaced by "transactivator"), thereby obviating this part of the rejection.

Claims 4 and 8 are considered by the examiner to remain indefinite because the examiner holds that PC12 pheochromocytoma cells and N2a neuroblastoma are not "neuronal cells". It should be emphasized that these cells can respond by differentiating into cells with all the same properties of "real" neurons, i.e., electrical excitability, release of neurotransmitters, and neurite outgrowth. Nevertheless, this part of the rejection is obviated by the amendment to the claims to recite treating or culturing PC12 cells or N2a neuroblastoma cells as alternatives to neuronal cells.

The Fan et al., Dickey et al., Greene et al., and Prenzel et al. references cited and attached to the amendment of April 28, 2005, were only submitted as evidence of patentability and not as prior art references considered "material" to patentability. Applicants are not seeking to have these references listed on the front page of a U.S. patent as being considered material to patentability; rather, they were submitted merely to provide evidentiary support for arguments rebutting an indefiniteness rejection. Accordingly, such references need not be submitted in an Information Disclosure Statement in order to be considered.

While applicants do not agree that the term "small" is indefinite, even though it is a relative term and there is case law concerning whether or not the term "small" is indefinite, this issue is made moot by the deletion of the term "small" from the present claims.

This third step of assay A in claim 1 is amended as suggested by the examiner, thereby obviating this part of the rejection.

Regarding the indefiniteness of claim 1 (assay C) and claims 10 and 12 (assay B), the recitation of "to provide an assessment of the relative level of phosphosylated Akt and the extent of activation" is deleted from claims 10 and 12 and claim 1 (assay C) is amended to recite that an increase in cell survival (or conversely a decrease in cell death) over a control in which the cells are cultured in the absence of neurotrophic factors and the candidate transactivator molecule, identifies a transactivator molecule", thereby obviating this part of the rejection. The recitation added to claim 1 (assay C) is supported by Figs. 6A and 6B and the present specification discussing these figures at page 39. The control is in the absence of neurotrophic factors and the candidate transactivator molecule. The amendment to claim 1 (assay C) was not presented earlier because this part of claim was previously considered withdrawn and unexamined. It is only for the final Office Action

of August 29, 2005, that this part of claim 1 was examined for the first time. Therefore, this is the first opportunity that applicants have had to address this indefiniteness issue raised by the examiner. Accordingly, entry of this amendment is respectfully requested.

The term "specific", as it refers to binding, is now deleted from claims 9 and 11, thereby obviating this part of the rejection.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1-4 and 9-12 have been rejected under 35 U.S.C. §102(b) as being anticipated by Clary et al., U.S. Patent 5,753,225. This rejection is respectfully traversed.

It appears to applicants that this rejection is maintained partly or wholly because of the overlooked instance of reciting treating neuronal cells with a candidate small molecule "activator" instead of "transactivator" as intended in base claim 1 (assay A). As discussed above in the indefiniteness rejection, all recitation of "activators" in the claim have now been amended to "transactivator" to make clear that the present invention involves transactivation (well understood in the art as being activated from afar or from a distance) and not direct activation as disclosed by Clary.

Clary teaches at column 4, line 66 to column 5, line 3 and at column 6, lines 27-31, that immunoglobulins of Clary's invention mimic the actions of neurotrophins and activate the receptor (activation observed/assayed as tyrosine phosphorylation of trk receptors - see column 11, lines 65-67 and Example 4 at columns 27-28) by what is thought to be allosteric dimerization such that tyrosine kinase receptors form oligomers in response to binding by neurotrophin (or to a bivalent or polyvalent immunoglobulin that mimic the action of neurotrophins, according to Clary's invention - see column 7, lines 49-52). Thus, Example 4 of Clary teaches that a bivalent anti-trkA antibody, RtrkA.Ex IgG, physically binds to and dimerizes trkA receptors to stimulate protein tyrosine phosphorylation of the trkA receptor in the absence of NGF. It is abundantly clear to one of ordinary skill in the art from the disclosures and teachings of Clary that the anti-trkA antibody RtrkA.Ex IgG binds to the trkA receptor to dimerize and <u>directly</u> activate the receptor.

By contrast, the present invention as recited in the claims requires <u>transactivation</u>, which is distinct from direct <u>activation</u>, because the transactivator transactivates indirectly from a distance rather than directly on the neurotrophin receptor to dimerize and activate, such as by neurotrophins and the immunoglobulins of Clary, as would be well understood by one of ordinary skill in the art. Accordingly, Clary simply does not

and cannot anticipate or make obvious the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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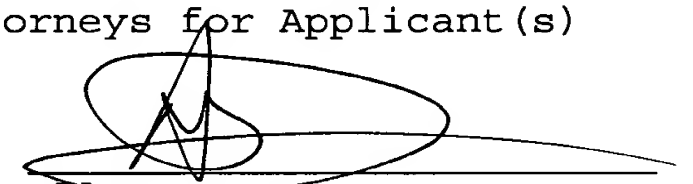
By 
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